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| EXAMINER | |
|---|---|
| DAVIS, MINH TAM B | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/973,382 | Applicant(s) HESTON ET AL. | |
|---|---|---|---|
| | Examiner MINH-TAM DAVIS | Art Unit 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *8-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4, 6-7* is/are rejected.

7)☒ Claim(s) *3 and 5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's election without traverse of group I, claims 1-7, in Paper No.6 is acknowledged and entered.

Claims 1-42 are pending in the instant application and Claims 8-42 have been with drawn from further consideration by the Examiner under 37 CFR 1.142(b) as being drawn to non-elected invention.

Accordingly, group I, claims 1-7 are examined in the instant application.

## OBJECTION

1. The specification is objected to because pages 41-42 in the instant specification are empty space.

2. The specification is objected to because the cross-reference to related application recited on the first page of the specification does not include as a CIP the prior application PCT/US 00/09417, filed 04/09/2000, as indicated in the Application of 10/09/2001.

3. Claim 2 is objected to, because it is not clear whether fragments thereof are fragments of SEQ ID NO:1 or fragments of the DNA fragment of claim 1.

4. Claim 3 is objected to, because it is not clear whether fragments thereof are fragments of SEQ ID NO:2 or fragments of the DNA fragment of claim 1.

5. Claims 3, 5 appear to be free of prior art but are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent forms.

## REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 1, 4, 6-7 are rejected under 35 USC 112, first paragraph.

Claims 1, 4, 6-7 are drawn to:

1) A DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", selected from the group consisting of:

a) an isolated DNA fragment which encodes a "prostate specific membrane antigen-like protein",

b) an isolated DNA fragment which "hybridizes" to the isolated DNA fragment of (a) above, and which encodes a "prostate specific membrane antigen-like protein",

c) an isolated DNA fragment differing from the DNA fragment of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a "prostate specific membrane antigen-like protein" (claim 1),

2) A vector comprising the DNA fragment of claim 1 (claim 4), and

3) A host cell transfected with said vector, wherein said cell is selected from the group consisting of a bacterial cell, a mammalian cell, a plant cell and an insect cell (claims 6, 7).

The specification discloses that a gene highly similar to but distinct from the prostate specific membrane antigen (PSMA) is designated as "PSMA-like" gene (p.15, lines 14-15). The specification further discloses that preferably, the PSMA-like protein

has an amino acid sequence shown in SEQ ID NO:2 or fragments thereof (p.9, lines 11-12). The specification discloses that PSMA-like gene is isolated from a liver library, and the complete sequence is shown in SEQ ID NO:1 (p.45, lines 9-10).

No clear definition of prostate specific membrane antigen-like gene is found in the specification, nor it is not clear how similar is highly similar.

It is noted that since there is no clear definition of a prostate specific membrane antigen-"like" gene, nor a clear definition of highly similar, a DNA fragment encoding a "prostate specific membrane antigen-like protein" could be reasonably interpreted as any gene that is "highly similar" to but distinct from the prostate specific membrane antigen, and variants thereof, i.e. **variants of a nucleic acid molecule encoding the prostate specific membrane antigen, with unknown structure and function**. Further, a DNA fragment encoding a "mammalian" prostate specific membrane antigen-like protein" could be reasonably interpreted as variants of the DNA encoding a prostate specific membrane antigen **from any mammalian species, such as human, mice, rat, pig, monkey etc...**

In addition, a DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein" encompasses a DNA fragment encoding a wild type mammalian prostate specific membrane antigen-like protein, or variants thereof.

Further, an isolated DNA fragment which "hybridizes" to the isolated DNA fragment encoding a "prostate specific membrane antigen-like protein", and which encodes a "prostate specific membrane antigen-like protein", encompasses DNA fragments which binds to variants of a nucleic acid molecule encoding the prostate specific membrane antigen, with unknown structure and function, and which encodes

**variants of a nucleic acid molecule encoding the prostat specific membrane antigen, with unknown structure and function**, since an isolated DNA fragment which encodes a "prostate specific membrane antigen-like protein" encompasses variants of a nucleic acid molecule encoding the prostate specific membrane antigen, with unknown structure and function, *supra*.

The findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are clearly relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated,

does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

Thus, the instant specification may provide an adequate written description of the DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", per Lilly by structurally describing a representative number of DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", or by

describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein" required to practice the method of claims 1, 4, 6-7 in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein" other than SEQ ID NO:1, nor does the specification provide any partial common structure of such DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", nor any physical or chemical characteristics of the DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", SEQ ID NO:1, this does not provide a description of transcytosis receptors to which the claimed synthetic cross-linker protein is capable of binding that would satisfy the standard set out in Enzo.

The specification also fails to describe the DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein"to which the claims synthetic cross-linker protein is capable of binding by the test set out in Lilly. The

specification describes only a single DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", SEQ ID NO:1. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein" that is required to practice the claimed invention.

**REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE**

**1.** Claims 1, 4, 6-7 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide sequence shown in SEQ ID NO:1, or a polynucleotide sequence encoding SEQ ID NO:2, **does not reasonably provide enablement for a DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein" and hybridizing species thereof that encodes a "mammalian prostate specific membrane antigen-like protein".** The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 4, 6-7 are drawn to:

1) A DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", selected from the group consisting of:

a) an isolated DNA fragment which encodes a "prostate specific membrane antigen-like protein",

b) an isolated DNA fragment which "hybridizes" to the isolated DNA fragment of (a) above, and which encodes a "prostate specific membrane antigen-like protein",

c) an isolated DNA fragment differing from the DNA fragment of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a "prostate specific membrane antigen-like protein" (claim 1),

2) A vector comprising the DNA fragment of claim 1 (claim 4), and

3) A host cell transfected with said vector, wherein (claims 6, 7).

It is noted that since there is no clear definition of a prostate specific membrane antigen-"like" gene, nor a clear definition of highly similar, a DNA fragment encoding a "prostate specific membrane antigen-like protein" could be reasonably interpreted as any gene that is "highly similar" to but distinct from the prostate specific membrane antigen, and variants thereof, i.e. **variants of a nucleic acid molecule encoding the prostate specific membrane antigen, with unknown structure and function**. Further, a DNA fragment encoding a "mammalian" prostate specific membrane antigen-like protein" could be reasonably interpreted as variants of the DNA encoding a prostate specific membrane antigen **from any mammalian species, such as human, mice, rat, pig, monkey etc...**

In addition, a DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein" encompasses a DNA fragment encoding a wild type mammalian prostate specific membrane antigen-like protein, or variants thereof.

Further, an isolated DNA fragment which "hybridizes" to the isolated DNA fragment encoding a "prostate specific membrane antigen-like protein", and which encodes a "prostate specific membrane antigen-like protein", encompasses DNA fragments which binds to variants of a nucleic acid molecule encoding the prostate specific membrane antigen, with unknown structure and function, and which encodes **variants of a nucleic acid molecule encoding the prostate specific membrane antigen, with unknown structure and function**, since an isolated DNA fragment which encodes a "prostate specific membrane antigen-like protein" encompasses variants of a nucleic acid molecule encoding the prostate specific membrane antigen, with unknown structure and function, *supra.*

The scope of the claims 1,4, 6-7 includes numerous structural variants. Applicants have not shown how to make and use the claimed variants which are capable of functioning or have the properties of the polynucleotide of SEQ ID NO:1, as that which is being disclosed.

The claims read on a variant nucleotide sequence encoding a variant of the polypeptide encoded by SEQ ID NO:1, wherein said variant has any type of substitution besides conservative substitution, at any amino acid, throughout the length of the peptide, as well as insertions and deletions. The specification and the claims do not place any limit on which amino acid to be subjected to conservative or non-conservative substitution, the type of substitution besides conservative substitution, nor the type of amino acids replacing the original amino acids. In addition, the specification and all other pending claims do not place any limit on the number of amino acids that could be substituted. Thus the scope of the claims includes nucleotide sequences encoding

numerous structural variants. Although the types of changes are routinely done in the art, the specification and the claims do not provide any guidance as to which, or how many original amino acid(s) to be substituted, or to which type of substitution besides conservative substitution, or which amino acids could be deleted or inserted in the encoded polypeptide, so that the claimed polynucleotide and the encoded polypeptide could function as contemplated.

One cannot extrapolate the teaching in the specification to the scope of the claims because one cannot predict that the claimed variants of SEQ ID NO:1 would have properties related to that of SEQ ID NO:1. The following teaching of the art, although drawn to proteins, would apply as well the claimed polynucleotide variants of SEQ ID NO:1, because polynucleotide sequences encode proteins. It is well known in the art that protein chemistry is probably one of the most unpredictable areas of biotechnology and that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. For example, Bowie et al (Science, 1990, 257 : 1306-1310) teach that an amino acid sequence encodes a message that determine the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instruction of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (col.1, p.1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid

substitution can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col.2, p.1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al, (Journal of Cell Biology, 1990, 11: 2129-2138), who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

The specification does not disclose how to make the claimed nucleic acid molecules, such that they would function or have the properties as claimed, or how to use said nucleic acid molecules if they did not have the function or properties claimed.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or

use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the unpredictability that the claimed variants would have the property or function of SEQ ID NO:1 , the lack of adequate disclosure in the specification on how to make such variants, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

**2.** Claims 6-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated host cell transfected with a vector comprising the polynucleotide of SEQ ID NO:1, **does not reasonably provide enablement for "a host cell"** transfected with a vector comprising a DNA encoding a mammalian prostate specific membrane antigen-like protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 6-7 are drawn to a host cell transfected with a vector comprising a DNA fragment encoding a mammalian prostate specific membrane antigen-like protein, selected from the group consisting of:

a) an isolated DNA fragment which encodes a "prostate specific membrane antigen-like protein",

b) an isolated DNA fragment which "hybridizes" to the isolated DNA fragment of (a) above, and which encodes a "prostate specific membrane antigen-like protein",

c) an isolated DNA fragment differing from the DNA fragment of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a "prostate specific membrane antigen-like protein". Said host cell is a mammalian host cell.

The specification contemplates a method of inducing cell death, wherein said cell is a prostate cancer cell, comprising transfecting said cell with a vector expressing PSMA-like protein (claims 38-39, p. 22, last paragraph). The specification further discloses that the transforming DNA in a cell transfected with the claimed polynucleotide may be integrated into the genome of the cell (p.30, lines 8-9).

In view of the disclosure in the specification, the claim encompass an in vivo host cell.

One cannot extrapolate the teaching in the specification to the scope of the claim for the following reasons: The state of the gene therapy art at the time of filing was that the combination of vector, promoter, protein, cell, target tissue, level of expression and route of administration required to target the tissue of interest and obtain a therapeutic effect using gene therapy was unpredictable. For example, Miller (1995, FASEB J., Vol. 9, pages 190-199) review the types of vectors available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated

into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and indicates that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

Thus in view of the teaching in the art that gene therapy is unpredictable, and the lack of disclosure of any objective evidence concerning obtaining in vivo host cell transfected with the claimed polynucleotide, it would be undue experimentation for one of skill in the art to practice the claimed invention.

**REJECTION UNDER 35 USC 102 (b or e)**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

**1.** Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Su SL et al, 1995, Cancer Res, 55: 1441-1443,.

Claim 1 is drawn to a DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", selected from the group consisting of:

a) an isolated DNA fragment which encodes a "prostate specific membrane antigen-like protein",

b) an isolated DNA fragment which hybridizes to the isolated DNA fragment of (a) above, and which encodes a "prostate specific membrane antigen-like protein",

c) an isolated DNA fragment differing from the DNA fragment of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a "prostate specific membrane antigen-like protein".

It is noted that the specification does not define "mammalian prostate specific membrane antigen-like (PSMA-like) antigen in any limiting way. Thus it is assumed for the purpose of compact prosecution that any nucleic acid that encodes a protein that is related to PSMA is a nucleic acid encoding a PSMA-like protein.

Su et al teach an alternatively spliced variant of prostate-specific membrane antigen (PSM) RNA (abstract and figure 1). Su et al further teach that the variant is shorter than the wild type PSM .

It is noted that the splice variant of prostate-specific membrane antigen is related to prostate-specific membrane antigen but is not identical to it. Thus a nucleic acid encoding the splice variant of prostate-specific membrane antigen would encode a PSMA-like protein.

The reference does not specifically teach a DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", However, the claimed DNA fragment appears to be the same as the nucleic acid taught by the art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of

evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Further, given the variant of prostate-specific membrane antigen taught by Su et al, one would readily envision its hybridizing species, and a DNA fragment differing from the above nucleotide sequence in codon sequence due to the degeneracy of the genetic code, and which encodes a prostate specific membrane antigen-like protein.

**2.** Claims 1, 4, 6-7 is rejected under 35 U.S.C. 102(e) as being anticipated by US 6,387,888 B1.

Claim 1 is drawn to a DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", selected from the group consisting of:

a) an isolated DNA fragment which encodes a "prostate specific membrane antigen-like protein",

b) an isolated DNA fragment which hybridizes to the isolated DNA fragment of (a) above, and which encodes a "prostate specific membrane antigen-like protein",

c) an isolated DNA fragment differing from the DNA fragment of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a "prostate specific membrane antigen-like protein".

Claims 4,6-7 are drawn to a vector comprising a DNA fragment encoding a mammalian prostate specific membrane antigen-like protein of claim 1, and regulatory elements necessary for expression of the DNA in a cell, a host cell transfected with said

vector, wherein said vector expresses a prostate specific membrane antigen-like protein, and wherein said cell is selected from the group consisting of a bacterial cell, a mammalian cell, a plant cell and an insect cell.

US 6,387,888 B1 teaches a polynucleotide encoding a truncated form of human prostate specific membrane antigen (PMSA), comprising the extracellular domain of PMSA, and lacking functional transmembrane and cytoplasmic domain (claim 1).

US 6,387,888 B1 further teaches cloning of said truncated form of PMSA into a mammalian expression vector, which is a plasmid or a propagation deficient virus (column 4, lines 48-53). US 6,387,888 B1 teaches that the vector provides human CMV promoter/enhancer region permitting efficient, high level expression of recombinant protein (column 5, lines 37-46). US 6,387,888 B1 teaches that dendritic cells from healthy donor or patients are prepared by transfected with either the plasmid or the propagation deficient virus (column 4, lines 53-58,column 6, lines 25-26, lines 56-57), and that expression of PSMA in DCs cells are tested by immunoblotting (column 6, lines 53-54).

The polynucleotide encoding the truncated form of prostate-specific membrane antigen taught by US 6,387,888 B1 seems to be highly similar to but distinct from prostate-specific membrane antigen, and thus seems to be the same as the claimed DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein.

The reference does not specifically teach a DNA fragment encoding a "mammalian prostate specific membrane antigen-like protein", However, the claimed DNA fragment appears to be the same as the nucleotide sequence taught by the art. The office does not have the facilities and resources to provide the factual evidence

needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Further, given the variant of prostate-specific membrane antigen taught by US 6,387888 B1, one would readily envision its hybridizing species, and a DNA fragment differing from the above nucleotide sequence in codon sequence due to the degeneracy of the genetic code, and which encodes a prostate specific membrane antigen-like protein.

In addition, the claimed vector and host cell seem to be the same as the vector and host cell taught by US 6,387888 B1.

**3.** Claim 2 is rejected under 35 U.S.C. 102( e) as being anticipated by US 5,962,237.

Claim 2 is drawn to a DNA fragment encoding a mammalian prostate specific membrane antigen-like protein, wherein said DNA fragment has the sequence shown in SEQ ID NO:1 or "fragments" thereof.

US 5,962,237 teaches SEQ ID NO:6, which is 50 nucleotides in length, and is 100% similar to nucleotides 1352-1401 of the claimed SEQ ID NO:1, under MPSRCH sequence similarity search (MPSRCH search report, 2004, us-09-973-382c-1.oli.rni, p.7).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

PATENT EXAMINER

December 12, 2003